literature the differentiation between salivary gland dysfunction due to cGVHD and long-term related high dose chemotherapy.

Table. *Preliminary Results of Gallium-67 Scintigraphic Study on Major Salivary Glands (n = 18 patients)*

	Submandible (n patients)		Parotid (n patients)	
	Positive	Negative	Positive	Negative
Before BMT	1	17	0	18
Day +30 after	5	9	3	11
Day + 60 after	7	6	3	10
Day + 100 after	7	6	4	9

LYMPHOMA/MULTIPLE MYELOMA

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A PILOT STUDY OF MYELOABLATIVE (MA) AUTOLOGOUS STEM CELL TRANSPLANTATION (AUTOSCT) FOLLOWED BY REDUCED INTENSITY (RI) ALLOGENEIC TRANSPLANTATION (ALLOSCT) IN CHILDREN AND YOUNG ADULTS WITH RELAPSED/REFRACTORY LYMPHOMA

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AlloSCT may be beneficial to patients with relapsed Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL) by providing a graft vs HD effect. MA AlloSCT is however associated with a high incidence of regimen-related mortality (RRM) (Jones et al, Blood 77:649, 1991). Carella et al (JCO 18:3918, 2000) demonstrated the feasibility of MA AutoSCT followed by RI AlloSCT in adults with refractory HD. We investigated MA AutoSCT followed by RI AlloSCT in relapsed pediatric HD/NHL. Patients were entered post reinduction therapy (2 CR + 2 PR after Ifos/Carbo/Etop, 1 CR after Ifos/Vinorelbine and 1 PR after Topo/Ifos/Carbo). MA: Cyclo 1500 mg/m^2 × 4d, BCNU 100 mg/m^2 × 3d, VP-16 800 mg/m^2 × 3d, and AutoSCT. Patients with CD20$^+$ lymphoma (5/6) received Rituximab (375 mg/m^2/wk/×4) and 6 patients received IFRT (2-3 Gy). RI: Flu 30 mg/m^2 × 5d, Bu 3.2 mg/kg × 2d, and Thymoglobulin® 2.0 mg/kg × 4d (UCB recipients only) and AlloSCT (1 related 6/6 PBSC, 5 4/6 UCB). GVHD prophylaxis: FK506 (0.03 mg/kg CIVI) on day-1-+60 and MMF (15 mg/kg) day +1-+28. Five HD age 13-21 yrs, 2 stage IIA, 1 stage IIIB, 1 stage IVA, 1 stage IVB and 1 stage III ALCL, age 11, have been treated. MA AutoSCT + RI AlloSCT were well tolerated in all patients. Median time to RI AlloSCT after MA AutoSCT was 121 d. Median F/U is 577 d. Toxicity: grade 3 hematuria (n = 1), grade 3/4 infection without neutropenia (n = 3), grade 4 infection with neutropenia (n = 2), grade 4 pulmonary fibrosis (n = 1), grade 4 hearing loss (n = 1) and grade 4 thrombocytopenia (n = 1). Following RI AlloSCT, myeloid recovery occurred on day +15 (MRD), day +18, +23, +15, +30, +45 days (UCBT), platelet recovery on day +11 (MRD), day +31, +170, +25, +62, NE (UCBT). All patients achieved 100% donor chimerism by d+180. HD patients: 4/5 are NED at d +837, +836, +632 (deceased) and +147, respectively, 1/5 PD d +175. NHL: NED at d +522. One patient developed grade II AGVHD of the gut which resolved with steroids. One patient developed limited CGVHD which responded to alternating CSA + Pred. One pt developed extensive CGVHD. There has been one death (NRM) from infection d +632. The estimated OS at 1 year is 100%. In summary, MA + AutoSCT followed by IFRT, targeted monoclonal antibody therapy, and RI AlloSCT is feasible and well tolerated in pediatric patients with relapsed HD/NHL. A larger controlled study with longer follow up is required to determine if this approach will reduce relapse and/or long-term toxicity and improve EFS.

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PERSISTENTLY LOW SERUM OSTEOPROTEGRIN LEVELS DURING THE TREATMENT OF MULTIPLE MYELOMA PATIENTS PREDICTS WORSE EVENT-FREE SURVIVAL

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Osteoprotegrin (OPG) functions as a secreted inhibitor of bone resorption and its serum levels have been reported to be reduced in patients with multiple myeloma (MM). In this study, serum and urine OPG levels were prospectively measured in patients with MM (stage II III) and in patients with other hematologic malignancies (control group) and correlated to response to therapy. Newly diagnosed as well as patients on maintenance therapy were included. The MM and control group were well matched in terms of age and gender, as well as time from diagnosis to enrollment. Seventeen MM patients underwent autologous stem cell transplant while none in the control group were transplanted. Blood and urine samples were collected monthly, cytocentrifuged and stored in frozen aliquots at −20° C until analyzed. OPG was measured using an ELISA. Thus far data on 28 MM patients and 9 patients with other hematologic malignancies (2 AML, 2 CML, 1 CLL, 2 NHL, 2 monoclonal gammopathy of unknown significance) have been analyzed. All patients were treated with monthly intravenous bisphosphonate. The results reveal that OPG is detectable in the urine and its levels correlate significantly (r = 0.77 and two-tailed $P = 0.0032$) with the degree of renal failure as reflected by serum creatinine. Our results also show that the overall median serum OPG level was lower in MM patients (1181 pg/mL), but not significantly different than that of the control group (1437 pg/mL). However, 4 of 20 (20%) evaluable MM patients with adequate follow-up had OPG serum levels that remained < 1000 pg/mL throughout the treatment. Their median event-free survival (EFS) was 8 months compared with 19 months for the rest of the group ($P = 0.023$), while no significant difference was detected in the median overall survival. There was no OPG serum levels < 1000 pg/mL during the follow-up of the control group. Among the 10 newly diagnosed MM patients enrolled in the study, only 2 (20%) had low serum OPG at presentation, with no detectable urine OPG. Median OPG serum levels were lower for MM patients during induction therapy (940 pg/mL, n = 7) in comparison to those undergoing maintenance therapy (1536 pg/mL, n = 8; $P = 0.16$). In conclusion, OPG urine as well as serum levels should be monitored simultaneously since low serum levels may reflect high OPG urinary loss. In addition, persistently low OPG serum levels throughout treatment of MM patients may be a prognostic factor for worse EFS.

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ASCT IN A YOUNG PATIENT WITH FEATURES OF POEMS SYNDROME EVOLVING TO MULTIPLE MYELOMA

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POEMS syndrome is a rare plasma cell dyscrasia characterised by polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes. The pathogenesis of the disease is unclear. However, certain features are similar to multicentric Castleman's disease and HHV-8 infection. We report the case of a patient with POEMS syndrome progressing to multiple myeloma that was unresponsive to treatment with rituximab and standard chemotherapy but improved considerably after ASCT. The 28 year old patient presented with severe polyneuropathy. A low level IgG lamda monoclonal gradient and a slight plasma cell infiltration of the marrow was found. Hepatosplenomegaly, thrombocytosis, polycythemia, plethora and low TSH was consistent with POEMS syndrome. The patient had anti-HHV-8 antibodies and HHV-8-DNA was found in her initial marrow examination. While reported to be effective in Castleman's disease, the patient was treated with 4 doses of rituximab, but did not respond. During the following 3 months the patient progressed to multiple myeloma with a bone marrow involvement of > 20% plasma cells. Atypical plasma cells and a hypercellular megakaryopoesis were found. However, no

osteolytic or osteosclerotic bone lesions were detectable. HHV-8 DNA was no longer detectable in marrow or blood. The patient received 4 cycles of idarubicine/dexamethasone. The response to this treatment was minimal and an ASCT was planned. After mobilisation chemotherapy with iphosphamide, epirubicine and etoposide, 29.65 x 10^6 CD34-positive progenitor cells/kg could be harvested with one leukapheresis. ASCT was performed after high dose therapy with melphalan 200 mg/m^2. Reinfusion of 14.83 × 10^6 CD34-positive progenitor cells/kg and medication with G-CSF resulted in engraftment on day +9. Restaging 5 weeks later showed an excellent response. Bone marrow plasma cell infiltration was no longer detectable and hypercellularity of megakaryopoesis was markedly reduced. The platelet counts had returned to normal and the pleural effusions had vanished. IgG and serum electrophoresis were normal while the immunofixation remained positive for IgG lamda. The polyneuropathy of the patient is continuously improving. In conclusion, this case may represent an evolution from possibly HHV-8 related POEMS syndrome to multiple myeloma. Despite lack of response to standard chemo- and immunotherapy ASCT seems to be a useful therapeutic option in patients with signs of POEMS syndrome.

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RNA-LOADING OF CMRF-56 POSITIVE BLOOD DENDRITIC CELLS IS A PROMISING STRATEGY FOR MULTIPLE MYELOMA IMMUNOTHERAPY

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Immunologic responses to the malignant plasma cells of multiple myeloma (MM) patients are beinginvestigated for their ability to prevent disease relapse after autologous and allogeneic haematopoietic stem cell transplantation. Dendritic cells (DC) are specialized leukocytes that have the capacity to prime and direct an immune response against tumour-associated antigens (TAA). We have used new Trucount® technology to evaluate the whole blood DC subset composition of healthy donors and MM patients. MM donors have similar numbers of CD11c+ CD16+ and CD11c+CD16-blood DC subsets but about half the number of CD11c-CD123+ blood DC compared to normal donors. A CMRF-56 monoclonal antibody-based immunomagnetic selection procedure was used to enrich blood DC for functional studies from the peripheral blood mononuclear cells of healthy donors and MM patients. CMRF-56+ blood DC from MM patients are efficiently activated *ex vivo* and induce autologous and allogeneic mixed lymphocyte responses. The CMRF-56+ blood DC preparation is able to present MHC class I -restricted peptide antigens and has been used to generate cytotoxic T lymphocytes (CTL) against MM -related TAA, hTERT and MUC1. We have optimised the loading of CMRF -56+ blood DC preparations with antigen-encoding mRNA and have shown that enhanced green fluorescent protein mRNA is rapidly transl ated after electroporation into blood DC. In addition, influenza matrix protein (FMP) mRNA -loaded blood DC can process and present antigen to FMP-specific CTL clones and prime FMP-specific CTL responses in whole PBMC populations. We are currently in the process of generating responses against total RNA extracted from MM cell lines prior to initiating a clinical trial of RNA-loaded CMRF-56+ blood DC in patients.

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FREELITE™; A NEW LABORATORY TOOL TO AIDE IN MONITORING MULTIPLE MYELOMA AFTER TREATMENT

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Background: Multiple Myeloma (MM) is a diagnosis based on multiple parameters. Immunoglobulin levels, radiography, and bone marrow morphology are all evaluated for diagnosis and disease monitoring. Each test examines a different aspect of the disease. Conflicting values between these can obscure the disease picture. In addition, there are several subsets of MM depending on the immunoglobulin secreted. However, one thing is common to all but 5% of MM patients; an excess of free light chains is produced. A new laboratory test, Freelite™, easily and accurately measures free light chains in the serum. **Methods:** One hundred fifty patients with MM who had undergone treatment, some including bone marrow transplant, were prospectively examined. Fifty were patients treated for free light chain MM. Seventy-two were patients treated for IgG MM and 28 were patients treated for IgA secreting MM. The current serum free light chains were examined using Freelite™ and then correlated to the disease state as identified by consensus of bone marrow biopsy, flow cytometry and electrophoresis. **Results:** Thirty-seven of the 50 patients treated for free light chain MM currently had disease. All 37 had markedly elevated serum free light chain levels. The 13 remaining patients were diagnosed "negative" or "atypical" and 8 of these had elevated serum free light chain levels. Forty-six of 100 patients treated for IgG or IgA MM currently had disease. All 46 of these had elevated serum free light chain levels. Fifty-four were diagnosed "negative" or "atypical" and 30 had elevated serum free light chain levels. **Discussion:** In this broad analysis of the most common subtypes of MM, Freelite™ is 100% sensitive when correlated to MM diagnosed by our standard methods. The issue then becomes the decreased specificity (43%) due to false positives that are seen in every subset. This may well be detection of recurrent or residual disease not seen by our standard methods. Only close follow-up will determine if these "false positive" patients recur before the "true negative" patients. This sensitive and quick serum analysis may prove to be an excellent tool for monitoring MM patients after treatment.

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AUTOLOGOUS VERSUS ALLOGENEIC STEM CELL TRANSPLANT FOR MULTIPLE MYELOMA

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We report results of a comparative analysis of 87 patients with multiple myeloma, treated with either autologous PBSCT (n = 70) or allogeneic sibling donor myeloablative transplant (n = 17) using cyclophosphamide and fractionated TBI conditioning. Autologous transplant recipients were significantly older (median age 53 vs. 47 years, $p < .01$) and had a longer period between diagnosis and transplant (10.5 vs 7 months, $p = .03$). Autologous transplant led to lower transplant related mortality (TRM) of 4% (95% CI 0-36%) vs. 18% (0-9%) in the allogeneic patients at 100 days post transplant ($p = .02$). More frequent complete responses (CR) were seen in the allogeneic patients (64% (95% CI 37-91%) vs. 34% (95% CI 23-45%) in the autologous patients, $p = .09$). In the autologous patients, overall survival of 86% (95% CI 80-95%) at one year and 50% (95% CI 47-75%) at 4 years was seen vs. 64% (95% CI 40-87%) at one year and at 4 years in the allogeneic patients. In patients surviving beyond one year, survival was superior in the allogeneic transplant patients (100% (95% CI 100-100%) versus 58% (95% CI 41-75%) at 4 years, $p = .02$). The cumulative incidence of relapse showed a trend towards higher relapse in the autologous patients (73% (95% CI 55-90%) versus (37% (95% CI 11-63%) in allogeneic patients at 4 years, $p = .1$). In multiple regression analysis, attainment of a CR or PR pre transplant (OR 3.4, 95% CI 0.9-12.9, $p = .06$), ≤ 1 year between diagnosis and transplant (OR 3.8, 95% CI 1.1-13.8, $p = .04$), ≤ 2 regimens of chemotherapy (OR 8.3, 95% CI 2.2-31.3, $p < .01$) were associated with good response. Early transplant with ≤ 4 chemo cycles (RR of failure 0.5 (95% CI 0.2-0.9, $p = 0.04$) and attainment of CR or PR post transplant (RR 0.4 (95% CI 0.2-0.7, $p < 0.01$) was a significant predictor of good overall and progression free survival. Older age at transplant (RR 1.1, 95% CI 0.9-1.3, $p = .06$), allogeneic transplant (RR 11.0, 95% CI 2.3-53.7, $p < .01$), and > 4 cycles of pretransplant chemotherapy (RR 6.3, 95% CI 1.1-35.7, $p = .04$) were each significant predictors of high TRM. We observed good clinical tolerance of the myeloablative conditioning regimen fol-